DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 50-708/S-013
NDA 50-709/S-010

Fujisawa Healthcare, Inc. 04 SEP 2001
Attention: Donald E. Baker
Senior Director, Regulatory Affairs
Parkway North Center
Three Parkway North
Deerfield, IL 60015-2548

Dear Mr. Baker:

Please refer to your supplemental new drug applications dated October 2, 1998, received October 5, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prograf® (tacrolimus) Capsules and Prograf® (tacrolimus) Injection. We note that these applications are subject to the exemption provisions contained in section 125(d)(2) of Title I of the FDA Modernization Act of 1997.

We acknowledge receipt of your submissions dated May 31, 2000, received June 2, 2000, which constitute a complete response to our August 5, 1999 action letter.

These supplemental new drug applications provide for revisions to the labeling for Prograf® Capsules and Injection based on the following Phase 4 commitments:

1. Conduct a study to confirm the pharmacokinetics of Prograf® (tacrolimus) in patients with mild and severe hepatic dysfunction.

2. Submit for review on completion of the study data being currently collected in the ongoing study to determine the pharmacokinetics of Prograf® (tacrolimus) in patients with mild and severe hepatic dysfunction.

3. Conduct *in vivo* drug interaction studies to screen for possible interactions with drugs to be used concomitantly with Prograf® (tacrolimus). Based on the *in vitro* results, *in vivo* drug interaction studies with Akey@ drugs should be conducted.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling text for the package insert submitted May 31, 2000.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed to each application. Please individually mount ten of the copies on heavyweight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 50-708/S-013, 50-709/S-010." Approval of these submissions by FDA is not required before the labeling is used.

If a letter communicating important information about these drug products (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to these NDAs and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Matthew Bacho, Regulatory Project Manager, at (301) 827-2127.

Sincerely,

Mark J. Goldberger, M.D., M.P.H.
Director
Division of Special Pathogen and
Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research